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# PUBLIC HEALTH REPORTS.

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## THE CHOLERA SITUATION.

Cholera continues prevalent in Italy. Cases of the disease are being reported in Russia, especially in the southern Provinces. According to last advices the disease is still present at Marseille, France, and in the Province of Tarragona in Spain. The disease is present in Turkey in Europe and Asia. Six cases were reported among pilgrims at Beirut. On August 30 cholera was reported present at Kobe and Osaka in Japan, and on September 26 at Tunis in Northern Africa. After a lapse of a considerable period in which no cases were reported a case of the disease occurred in Manila, P. I., during the week ended July 29, and a small number of cases are being reported from the Philippine provinces.

A point of interest in connection with the case of cholera reported in Manila is that of seven contacts, all upon examination proved to be harboring the cholera organism and to be cholera carriers. All were isolated, and during a period of 10 days' detention none had developed clinical symptoms of the disease.

Emigrants from Italy are bacteriologically examined by medical officers of the Italian Government for the presence of cholera carriers before embarkation. Out of a total of 9,557 such examinations made 40 carriers have been found at Naples and one at Palermo.

No cholera carrier nor case of cholera has arrived at a port of the United States since August 18, 1911.

To meet the possible detouring of Italian immigrants to ports in other European countries orders have been issued requiring bacteriological examination of all Italian steerage passengers on arrival at a port in the United States without regard to the port from which they sailed in conformity with department circular No. 47, July 19, 1911.

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## THE SALIENT EPIDEMIOLOGICAL FEATURES OF PELLAGRA.

By C. H. LAVINDER, Passed Assistant Surgeon, United States Public Health and Marine-Hospital Service.

The developments of modern medicine have repeatedly shown the great value which is to be attached to epidemiologic studies as an aid in the elucidation of the etiology of disease. It seems remarkable that such studies are lacking for pellagra. Many important epidemiologic facts have been observed and recorded for this disease, but anything like complete and detailed studies do not as yet exist.

The only modern work of this kind which we possess is that of Sambon and that of Alessandrini. Both of these authors have made important contributions to the subject, but each was striving to establish his own hypothesis of the etiology of the malady. Their contributions therefore are necessarily wanting a certain judicial point of view which would have much increased their value.

It is to be observed, moreover, that the studies of these two authors were made exclusively in Italy, and that practically all recorded epidemiologic observations refer, if not to Italian pellagra, at least to the pellagra of southern Europe. Such observations are lacking for many places where the disease is known to be endemic, and we have none for the United States. If careful studies of this nature, both extensive and intensive, could be made for many places, a comparison of results would establish on a firmer basis many points of importance which are now obscure and might serve at least to give us a more definite idea as to the direction of our future work on the all important question of the etiology of this disease. Ultimately of course such studies must lead us back to the individual patient for completion.

It is intended to assemble in this paper, without very much discussion, the epidemiologic data we already possess regarding pellagra with the idea of trying to make some estimate of how incomplete these data are, and what indications they may perhaps show.

First with regard to *prevalence and geographic distribution*, it may be noted that the statistics of pellagra are for many reasons notoriously inaccurate, and the general geographic distribution of this disease is in all likelihood uncertain. Sambon's expression that our knowledge of its geographic restriction very likely represents only the limitations of our information as to its extent should be borne in mind.

At present in a general way the disease is probably most prevalent in Northern and Central Italy, Southern Roumania, the Austrian Tyrol, Southeast Hungary and the Southeast United States. Lower Egypt might, perhaps, be included. It has now been reported from various parts of the world, both in the Eastern and Western Hemispheres, but on the whole displays at least certain geographical limitations, although these are not easy to define with any degree of accuracy.

Roussel (1865) wrote as follows concerning the geographic distribution of pellagra: "Recently this malady has invaded new countries, and to-day it is found to the south of 47 degrees of north latitude, between 10 degrees of longitude west and even beyond 25 degrees of longitude east, meridian of Paris, extending over a long zone of the temperate region of Europe, from Cape Finisterre to the banks of the Sereth, across the Pyrenees provinces of Spain and of France, Upper and Central Italy, and, in the basin of the Danube, upon the eastern and southern slopes of the Carpathians, even to the frontiers of the Russian Empire."

Since this date the disease has been much more extensively reported, and may be even much more widely prevalent than present reports show: It may in a general way be said that pellagra is confined to tropical, southern north temperate, and northern south temperate zones, and perhaps nothing more definite can now be said in a general statement.

Its *local geographic distribution* presents more striking peculiarities. In Italy, for example, it has for generations been endemic in the northern and central parts of the peninsula, but has definitely spared southern and insular Italy, though endemic in the island of Corfu, just across the Adriatic. In recent years, however, it appears to be slowly advancing southward. In Roumania, on the other hand, long endemic in the south, it now appears to be slowly traveling northward. It is endemic in Northern Italy and in the Austrian Tyrol, yet contiguous Switzerland and Germany have always escaped. Again, endemic and quite prevalent in Lower Egypt, it is comparatively rare and sporadic in Upper Egypt. In the United States, also, there seems a certain geographic restriction to the southeastern States.

Such sharp limitations are not constant, however. From Roumania it has apparently invaded neighboring parts of Russia and of Austria-Hungary, and is scattered along the Danube.

Without attempting any exhaustive statement of these peculiar and sharp limitations a glance at a map will show that such peculiarities are evident and striking. One other fact may be noted here, and that is the practical disappearance of the disease from France where it was once endemic and rather widely prevalent. In Spain, too, the disease has never seemed to spread widely.

It is not to be forgotten in this connection that the "zeist" idea of the etiology of pellagra has been so widely accepted that practically all pellagra literature bears more or less the coloring of this theory. Geographical observations have likewise not escaped this bias, and conclusions are not infrequently drawn which a strict estimation of facts do not entirely warrant. The statement that pellagra occurs only in those countries which grow and to a large extent subsist on maize products is, in itself, not only a statement of a very general nature, but is so wide as to include perhaps too much. Corn is grown and used as an article of food so extensively over the earth's surface that it might, with similar reason perhaps, be adduced as an etiologic factor in other diseases as well as pellagra. In other words, a premise of this character is so broad that it weakens the conclusion.

Among other general factors *climate* seems to exert no especial influence, though, as noted above, the disease seems to be confined to the tropical and the warmer parts of the temperate zones. The influence of climatic factors on the spoiling of corn are important, as is well known. *Seasonal influences* to the "zeists" are also of great importance for similar reasons. The relation between symptomatology and seasons is discussed later.

*Meteorologic and telluric conditions*, outside of their well-known relation to the corn theory, appear to present nothing noteworthy; although many of the older writers have paid a good deal of attention to excessive moisture, dryness, etc. The relation of the erythema to sunshine is mentioned later.

The *topographical distribution* of the disease has, in the opinion of most observers, furnished no facts of importance. In the recent work of Sambon, however, in support of his simulum theory of pellagra, great stress has been placed on topographic distribution. This forms an essential feature of this hypothesis. His observations go to show that the disease is linked to the swiftly running streams of hilly territory in which the simulum breeds.

It is certainly remarkable and striking to find, as we constantly do in the Italian reports, certain comparatively small areas in the midst of a large endemic section, reported as free of the disease; or certain other areas, contiguous to endemic regions, yet never reporting it.

Investigating pellagra in Italy I have been frequently impressed with the statements of practitioners in pellagrous sections that all of their cases come from this or that restricted locality.

Alessandrini, in his work, has also reported this peculiar "patchy" distribution of the disease.

Disregarding all etiologic theories, evidence is accumulating that the disease is one of locality or place. If established, this is a very important observation. Further reference is made to this later.

One or two of the older Italian authors have also tried to show that the disease did not occur along the seacoast, but subsequent observation has not entirely sustained this.

One very striking fact may be included here, which has been confirmed by all observers of European pellagra. Pellagra is largely rural, and rarely urban. It is the agricultural, rural classes, the poor peasants of Italy and other parts of Europe, who have borne the brunt of its ravages. The city dweller, poor and rich alike, has always, to a large extent, escaped. In a trip through northern and central Italy recently I took pains to make close inquiries and observations regarding this point and always received marked proof of its confirmation. The disease does occur in the cities rarely but the cases are so few as practically to be negligible.

This has always seemed to be a constant feature of pellagra, but, so far as reports show, it is not true of the disease in the United States. Men with the most extensive experience believe that the small, mill towns and villages of the Southern States suffer worst from the disease. Of course such a radical difference must await fuller observations for its confirmation.

*Economic and hygienic conditions, and food supplies.*—It is of course a general biologic law that poor economic and hygienic conditions, with bad water and poor food, are important factors in the production of disease, but these factors have more than this general significance with regard to pellagra.

Ever since pellagra was first described all have united in condemning the wretched conditions under which sufferers from this malady have been found to exist, as well as the poor quality of their food supply. In Europe pellagra is practically limited not only to the agricultural classes, but to the poorest of these classes. It is those who are poorly clothed, badly housed, and miserably fed; it is those who live in the greatest poverty and subsist on a diet which is unvaried in its monotony, often insufficient in quantity, badly prepared, and not infrequently of the poorest quality. Largely for these reasons the disease has received a sinister reputation and is confessed with shame.

This apparent relation of the disease to the character of the food supply has furnished the field for most of the etiologic theories and speculations. Whether ultimately this shall prove to be an important etiologic factor or only one of numerous other factors remains to be determined. But the fact is not to be overlooked that in Europe the great majority of those who suffer from pellagra do have a poor food supply.

Again, in the United States this does not seem a marked feature of the disease.

The malady, however, does not always spare the well-to-do classes, urban or rural, even in Europe. Cases, and even severe cases, among the better classes are not of frequent occurrence nor are they of such great rarity. It is a circumstance to be remarked that in Europe occasionally certain isolated families, in easy circumstances, have been known to suffer severely from the disease for one or more generations. This may suggest hereditary influences but does not exclude local conditions as etiologic factors.

In the United States numerous cases are constantly being observed among the well-to-do classes. Statistics are as yet, however, lacking.

The *relation of the disease to water* has of late attracted much attention. As noted, it is an essential feature of Sambon's hypothesis. Alessandrini also has made it an essential part of his theory and claims that the disease is due to a water-borne nematode worm of the family *Filaridæ*, and is prevalent in those places which use polluted, surface waters. Siler and Nichols have directed attention to the frequent presence of amœbiasis in pellagrins and suggested a possible relation to water. Terni and Fiorani, in a way, have recently pointed out an apparent relation between pellagra and certain water courses in northern Italy. Some of the older authors also have expressed such ideas.

It is to be noticed that all of this brings the disease into relation with water, but the character of this relation, in the opinion of these observers, is diverse. This point demands further attention.

With regard to *age incidence* of the disease there is some discordance. It may be said, however, that pellagra occurs at all ages, including even the infant at the breast. The greater number of cases are found in the active period of adult life from about 20 to about 40 years of age. Children—even young children—do not escape, as many observers believe, but, as Neusser has pointed out, they seem to possess a certain tolerance for the disease, presenting often only a mild erythema with no constitutional disturbances whatever. With Sambon, in Italy, I have myself frequently made this same observation. Many cases in young children are being reported in the United States, and among them not infrequently are seen severe cases.

With regard to *sex*, it probably can not be denied that women suffer more than men, but the difference in Europe is not large; furthermore, it is to be observed that the preponderance of the female sex is found to occur during the active sexual period of life and is possibly due to the additional burden imposed by childbearing.

The statistics from which these conclusions are drawn are compiled from the agricultural classes of Italy and Roumania, largely; and the conditions of life, with regard to labor, are just as severe for the women as for the men. So that during the childbearing period the women are called upon to assume an added burden. The preponderance of females is by some also attributed to the additional factor of a more susceptible nervous system.

In the United States, although statistics are scant, it seems undoubted that there is a marked preponderance of females and, in the Southern States, negro females.

With regard to *race and nationality* there is observed no especial immunity or predisposition. It has been said in a general way that

the negro of the Southern United States is a marked sufferer from the disease; but here again statistics are lacking.

In the matter of *occupation* it is evident in Europe that the agricultural class—the field laborer—is the worst sufferer; and it has been further pointed out that it is the poorest of this class which is so much predisposed to this disease. It is somewhat difficult here to separate the several factors which might play a part.

It has been stated above that apparently in the United States the field laborer is not the worst sufferer from the disease.

The question of *heredity* in pellagra may be considered a debatable one. In a disease whose etiology is unknown this question is not always easy of determination. It has never been established, and very rarely, if ever, claimed, that children are born with the disease. It has been claimed by many that the children of pellagrous stock often show hereditary anomalies of degeneracy, and a predisposition to the disease. Indeed the general opinion is that pellagra is hereditary largely in the sense of a predisposition. Even this view, however, has met opposition at the hands of some observers of wide experience. It seems not unfair to say that heredity is at least open to some doubt.

*Is pellagra contagious?*—This is a question which was much discussed, and about which many doubts were expressed in the earlier history of the disease. Modern writers, however, have seemed to regard this question as determined, and most of them assert that the disease is not contagious.

There are undoubtedly sufficient observations to exclude any idea of its transmissibility in any direct way from person to person. One or two may be worth mention. At the pellagrosario at Mogliano Veneto, near Venice, Italy, where for many years large numbers of pellagrins have been treated (at present some 400 or 500 inmates with about 60 or 70 employees) no attendant or nurse has ever been known to develop the disease. Such observations could be multiplied. Neusser states that he has many times observed in a large family, all living under the same conditions, only one member sicken with severe pellagra while the rest remained in the best of health. Such an observation has been confirmed scores of times. Facts of this character certainly seem to exclude any idea of contagion in the strict sense of that word.

As to whether the disease may or may not be transmissible in some remote or indirect way may be, in the present state of its etiology, certainly open to question. It is the general belief that the disease is not communicable in any sense whatever. It may be repeated here, however, that at least in Italy and Roumania, it does possess the characteristic of slowly extending its area of endemicity. This characteristic, however, does not necessarily imply any idea of transmissibility.

In the United States several observers have again raised the question of contagion and affirmed a belief in its probability.

If one may speak at all of *immunity* in pellagra the disease does not appear ever to confer any individual immunity. On the contrary it has repeatedly been observed that apparent cures are often followed by recurrent phenomena of the disease either at close or more remote periods of time.

Pellagra may be classed as *endemic*, at times *epidemic*, but never *pandemic*. It is a disease peculiarly endemic in character, as has already been noted. At certain seasons or in certain years the number of those affected within the area of its endemicity may show a marked increase. In its history it has also appeared in new territory, often far remote from its known endemic areas, as, for example, its more or less recent occurrence in America. From these points of view it may deserve to be called epidemic, but it has never shown any of the characteristics which mark the great epidemic diseases, with their extensive ebb and flow.

Reference has already been made to the possibility of the *disease* being one of *place or locality*. Certain other similar things may be noted which seem to show that pellagra presents the characteristics of a "place infection" in the sense in which the expression has been used with regard to beriberi.

The recognition and early development of the disease in the United States has furnished more than one instance which might possibly lend color to such an idea. It will be recalled that the disease in America was first observed in insane asylums, and more than one asylum awoke suddenly to find a large percentage of its inmates suffering from this disease (although many of the first observations, in South Carolina, at least, were in cases who had pellagra on admission). Subsequent investigation showed that the disease had long been present among the inmates of, as well as the new admissions to, these institutions, and doubt was created as to just what percentage of the cases could be charged to development within the institution. The various factors in the situation have not all been untangled, and conclusions are difficult to form. From the history of these situations and a study of conditions, however, one is almost forced to admit that these occurrences present at least some analogy to the so-called "place infection" of beriberi.

In the area of its endemicity the disease often shows other queer turns in the peculiarity of its dissemination. Sometimes all of the members of a family or house may suffer from it; just as often, indeed oftener, only one or two. Alessandrini states, for example, that in certain parts of Italy in the examination of 269 families composed of 1,659 persons, only 274 pellagrins were found among them. Only 5 families had as many as 2 sick. Among them was one family of 21 persons which showed only 1 sick. Again, out of 119 families composed of 528 persons there were only 129 pellagrins; of these the families worst affected had, in one case, 2 sick out of 3; and in another, 3 out of 6. One family of 13 had only 1 sick. In my personal experience in the United States I have three times seen orphan asylums suffer severely from the disease, although in each instance the children seemed generally healthy, the food supply good and abundant, and nothing in local conditions to indicate any especial reason for poor health among the inmates. In almshouses I have seen cases at times, while the large State prison in Columbia, S. C., was, when inspected by Babcock and myself, found singularly free of pellagra, although the disease is very prevalent in the neighboring insane asylum, as well as through the state generally. Later I saw one case in a prisoner discharged from this penitentiary, and, strange to relate, he was a man of the better class and had not eaten prison



fare, but had received his food supply during his incarceration largely from relatives and friends. Another odd fact is the apparent immunity enjoyed by the Italian Army, which, since military service is compulsory, is recruited from all over the Kingdom. I have been assured by medical officers of the Italian Army that except on recruiting duty pellagra is a disease of which in their official life they see nothing. Pellagrins are not recruited. It is, however, reported, I am told, among the Carabinieri at times.

The *seasonal incidence* of pellagra is one of its well known and marked characteristics. With striking regularity its severe manifestations become apparent at two seasons of the year—spring and fall. This has furnished the opportunity for much etiologic speculation, and has raised the question of the relation between the pellagrous erythema and exposure to sunshine. Such a relationship is undeniable, but is by no means definitely understood.

*Do any of the domestic animals suffer from pellagra?* Despite assertions to the contrary, I do not think any unbiased individual can be convinced that such cases have ever been observed. Moreover in spite of the long series of feeding experiments in both domestic and laboratory animals no one has ever yet produced in them any morbid condition which agrees in any sense with human pellagra. Further, experiments on laboratory animals, including monkeys, by the injection of body fluids and tissues have likewise given no conclusive results.

With regard to the disease itself some facts of importance in this connection should be recorded.

So far as *clinical characteristics* are concerned pellagra is a general disease of marked chronicity with periodic exacerbations of a peculiar kind; also the intervention at times of certain very striking attacks of a fulminating nature—so-called typhoid pellagra and allied conditions. These acute incidents are very notable phenomena in the evolution of the disease and have always attracted much attention. Their nature is obscure.

Then in the inception and evolution of the disease what may we regard as its *earliest symptomatology*, or rather what particular system of the body seems to be first involved in the morbid process? This is a point on which writers do not agree. It is a matter of importance in some respects since it may lead us to a suspicion of where may be found the "infection atrium"—if I may use such a term without implying any etiologic deduction. Is it the gastro-intestinal tract? Is it the skin? Can it be the respiratory tract? We may at least say, however, that both from clinical and pathological data the morbid process displays its most marked and most essential effects upon the central nervous system.

Pellagra again is, in a sense, a *secondary disease*, a morbid process which, so to speak, engrafts itself upon some preceding morbid condition or depressed state. This is a fact too well supported to admit of denial.

Does the disease display any "*latency*" in the sense, for example, of the accepted "*latency*" of malaria? Such an observation has been made by some writers, but is by no means definitely established. It does seem undoubtedly true that an individual presenting typical pellagrous phenomena for one or more years may for an equally long

while cease to display active evidence of the disease, but whether this may be spoken of as "latency" or not is questionable.

The disease displays a very marked *variation in its virulence and intensity*. At present in America it is observed to run a more acute course, to display more evidences of an intense intoxication, and to give a much higher mortality. These same characteristics were noted by the early Italian, French, and Spanish writers. In Italy, however, now for a long while the intensity of the disease has been steadily diminishing, severe types are comparatively rare, and the mortality is much reduced. The interpretation of this change in the character of the disease is of course uncertain, but it may perhaps be inferred that the Italians have developed a partial immunity to pellagra. Certainly no other explanation seems so obvious. Moreover it is a matter of fact in Italy that in treatment change of diet and surroundings very frequently results in a cure, or a least an arrest of the disease. The Italian pellagrosarios, where the treatment is largely dietetic, obtain very fair results. This is not true, however, with the severe types of the disease seen in America. The important point is, what effect is produced on the disease by the administration of good food in sufficient quantity with change of surroundings? Is pellagra curable, at least in its less intense forms, by these means alone? Here too may be asked, what is the real result of arsenical treatment? Reports are very discordant.

Here also may be put the ever-present question in pellagrous etiology, Is there a "*pellagra without maize*"? As Sturli has said, even the most pronounced "zeist" could not possibly deny that such cases have occurred and do occur. There are many well-authenticated cases of undoubted pellagra which have never eaten maize. Such cases are, however, sporadic, and up to the present time endemic pellagra without maize is unknown unless one accepts such as occurring in parts of Spain. There is an endemic disease called pellagra, reported as occurring in parts of Spain, where corn is neither grown nor eaten, but the Italian pellagrologists refuse to accept this as undoubted pellagra until it is further investigated.

Is pellagra a *morbid entity* or do we include under this term *more than one morbid entity*? These suspicions have very naturally been engendered by the question of pseudo-pellagra. The disease is so characteristic and so consistent in its phenomena, its evolution, its geographic distribution and even in its morbid anatomy that it must be considered, in my opinion, a morbid entity. But, apart from etiologic consideration, if there exist other conditions or states deserving the dignity of the title pseudo-pellagra, as now used by writers on pellagra, the presumption may well be entertained that we are dealing with more than one morbid entity. This is a matter of essential importance, and demands the close attention of all students of pellagra. A British writer has recently expressed the opinion that sprue and pellagra are identical diseases.

The characteristics outlined above, uncertain as they are in part and incomplete as they are in their entirety do not permit of important inferences. The need for more complete and more accurate and detailed epidemiologic data is too evident for comment. Such studies at present are of paramount importance. Furthermore, it would also seem unwise to base theories on epidemiological data collected in only one country. While accurate data of this nature do not exist

for the United States there is nevertheless, as above pointed out, very good reason to believe that in many essential points pellagra in this country differs from that of Europe. Until wider studies are made the epidemiology of American pellagra is of course uncertain, but it must even now be taken into some consideration.

As for further inferences, it is interesting to note that, from these data, there is some analogy between beriberi and pellagra, and in both diseases there are analogous etiologic theories. At present, however, the rice theory of the cause of beriberi can certainly present a far stronger claim for acceptance than can the maize theory of the cause of pellagra. The data are too incomplete really to justify any conclusions of great consequence.

I can not conclude this paper without some expression of the great need which exists in the United States for more complete information regarding the prevalence of pellagra. The disease is not reportable, and the number of cases among us is unknown. Such information must come largely from the individual practitioner; and it is to be hoped that the importance of reporting pellagra may not be overlooked.

Epidemiologic observations are likewise of importance and worthy of careful attention by those who come into contact with individual cases.

Finally, I acknowledge my indebtedness to the general literature of pellagra, but it is not feasible to give individual references. The observations recorded have been collected from too many sources.

It is hoped that under the direction of the Surgeon General of the service this paper may soon be supplemented by more detailed studies of the epidemiology of this disease.